

## REMARKS

### Introductory Comments:

Claims 55, 56, 58-72, 74-87, and 99-102 were examined in the Office Action dated June 9, 2004.

Claims 55, 56, 58-72, 74-87, and 99-102 were rejected under 35 U.S.C. §112, first paragraph, as allegedly including new matter.

Claims 55, 56, 58-72, 74-87, and 99-102 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent No. 5,463,564 to Agrafiotis *et al.* in view of Uhlmann *et al.* (1990) further in view of U.S. Patent No. 5,639,603 to Dower *et al.*, taken further in view of either U.S. Patent No. 5,720,923 to Haff *et al.* or U.S. Patent No. 5,650,122 to Harris *et al.*

These rejections are traversed for the reasons discussed below.

### **Addressing the Examiner's Rejections**

#### **Rejections of the Claims Under 35 U.S.C. §112**

The Examiner has maintained the rejection of claims 55, 56, 58-72, 74-87, and 99-102 under 35 U.S.C. §112, first paragraph, as allegedly being amended to include new matter. The rejection is based on the Examiner's assertion that there is no support in the specification for the combination of thermodynamic property and the listed properties or subcombinations of those properties to control the relevant steps in the rejected claims. *See* Office Action mailed June 09, 2004 at 3-4.

The applicants traverse the rejection since the disclosure of the application as filed provides complete written support for the rejected claims. In step 300 (Figure 1) a list of

oligonucleotide sequences with the desired properties for activity testing is generated.

The flow of data and materials among the elements of step 300 is illustrated in the flow diagrams of Figures 4 and 5, and described in the specification at page 16, line 26 to page 21, line 26. The specification, as filed, provides for the evaluation of the thermodynamic properties (page 16, line 26, to page 19, line 6, Figure 4 (especially at steps 306, 347, and 348) and Figure 6). The list thus generated is shown in Figure 4 Step 348 (which list includes all oligonucleotide sequences having scores within a desired range). Thus the specification teaches in at least these portions the generating or evaluating according to thermodynamic property limitation of the rejected claims. The “at least one other criteria selected from targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence and combinations thereof” limitations of the rejected claims are explicitly taught in at least Figure 5, and the corresponding portions of the specification explaining those steps (*see, e.g.*, specification at page 20, line 24 through page 22, line 2).

Figure 5, Step 349 is a decision point that operates on the list of all oligonucleotide sequences having *inter alia* the claimed thermodynamic property, and optionally adds in the claimed criterion of “targeting to functional regions of target nucleic acid sequence.” This is described in the specification at page 20, line 24 to page 21, line 16 where targeting to functional regions of target nucleic acid sequence is discussed.

If the decision is taken in Step 349 to include the “targeting to functional regions of target nucleic acid sequence, then Steps 350 and 370 are performed further select oligonucleotide sequences directed against specific functional regions within the target.

However, if the decision is taken in Step 349 is no, then the selection of oligonucleotides proceeds to Step 375 to include the optional criterion of “uniform distribution to target nucleic acid sequences” as further described in the specification at page 21, line 17 through page 22, line 2. On page 21, lines 18-21, the specification states that a large number of oligonucleotide sequences may result from the process thus far, therefore, a decision is made whether or not to uniformly distribute the selected oligonucleotides along the target.

The “target accessibility” criterion is taught in at least Figure 4, Step 306, Figure 6, Step 309, and the specification at page 16, line 26 through page 17, line 1 (teaching that calculation of the free energy of target structure (Fig. 6, Step 309) is optional), page 17, lines 12-19, teaching the relationship between free energy of target structure target accessibility factors relating to target secondary structure, and page 19, lines 7 through 14, also teaching the relationship between target secondary structure and target accessibility.

According to the MPEP § 2163: “While there is no in haec verba requirement, newly added claim limitations must be supported in the specification through express, implicit, or inherent disclosure.” Thus, the specification does not have to literally recite the wording of the claims in order to fulfill the Written Description requirement. The Figures and specific sections of the disclosure discussed above implicitly or inherently provide support for both the “at least one other criteria” and the “combinations thereof” limitations as required to fulfill the Written Description requirement. As discussed above, the branch points represented by Figure 5 Steps 349 and 375, and the description in the specification at page 16, line 26 through page 17, line 1 (teaching that calculation of the free energy of target structure (Fig. 6, Step 309) is optional) indicate that any of the

criteria “target accessibility” “targeting to functional regions of target nucleic acid sequence” or “uniform distribution to target nucleic acid sequence” and “combinations thereof” are optionally included. Thus, the specification discloses embodiments in which the only criterion is “thermodynamic property” as well as embodiments that include “thermodynamic property” in combination one or more (*i.e.*, at least one) “other criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence and combinations thereof.” It is only the latter embodiments (*i.e.*, those that include at least one additional criterion) that are claimed.

Thus, taken together, the specification clearly provides support for the combination of thermodynamic property with one or more of target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence. The amendment to the claims was therefore not New Matter, and the Examiner is respectfully requested to withdraw the rejection.

#### **Rejections of the Claims Under 35 U.S.C. §103**

The Examiner has rejected claims 55, 56, 58-72, 74-87, and 99-102 under 35 U.S.C. §103(a) as allegedly being unpatentable over Agrafiotis *et al.* in view of Uhlmann *et al.* further in view of Dower *et al.*, taken further in view of either Haff *et al.* or Harris *et al.* The Examiner stated that the rejection was maintained in anticipation of removal of the New Matter thus leaving the claims rejected as before.

The applicants traverse the rejection and supporting remarks as the references cited by the Office do not teach or suggest the claimed invention. As discussed in detail

above, the amendments to the claims do not constitute New Matter. The currently pending claims for generating or evaluating compounds according to thermodynamic property and at least one other criteria selected from target accessibility, targeting to functional regions of target nucleic acid sequence, or uniform distribution to target nucleic acid sequence, and combinations thereof are not taught or suggested by the combination of the cited references, as discussed in the Office Action mailed on August 4, 2003. Therefore, the Office has not established a *prima facie* case of obviousness, and the Examiner is therefore respectfully requested to withdraw the rejection.

### CONCLUSION

Applicants respectfully submit that the claims define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Respectfully submitted,  
Cowser *et al.*

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